Infectious Diseases Society of America's

Statement by Andrew T. Pavia, MD, Concerning

Pandemic Influenza

Before the

Committee on Energy and Commerce

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Chairman Deal, Ranking Member Brown, and Members of the House Energy and Commerce Health Subcommittee, thank you for inviting the Infectious Diseases Society of America (IDSA) to present our views on the U.S. preparedness for pandemic influenza and to allow us to share with you our perspective on activities needed to strengthen the nation's current approach. I am Dr. Andrew T. Pavia, chair of IDSA's Task Force on Pandemic Influenza, and professor and chief of the Division of Pediatric Infectious Diseases at the University of Utah Health Sciences Center and Primary Children's Hospital.

IDSA represents nearly 8,000 infectious disease (ID) experts, many of whom administer the flu vaccine to patients, treat life-threatening complications of influenza, conduct vaccine and antiviral research, and implement influenza surveillance activities and other important influenza public health programs at the local, state, and federal levels. Let me be very clear from the onset: Although we are speaking on the same panel as our industry colleagues, our testimony is provided strictly for the good of public health and the patients whom we treat. IDSA is not here on behalf of the pharmaceutical or biotechnology industries nor is our advocacy financed in any way by industry.

IDSA Is Seriously Concerned About the Next Influenza Pandemic

Like our colleagues in federal government, we believe that the next influenza pandemic is imminent. These predictions are primarily based upon the historic intervals between outbreaks as well as the increased spread and ominous behavior of the H5N1 avian

influenza virus, which now is endemic among birds in much of Asia. We are very concerned that the H5N1 avian virus has shown the ability to mutate and has become capable of infecting mammals, including pigs, tigers, cats, and humans as well as birds. At least 97 confirmed human cases of H5N1 infections have been documented by the World Health Organization (WHO) since January 2004 with 53 deaths. A recent WHO consultants meeting found evidence of further mutation and a suggestion that person-to-person transmission might be occurring in Northern Vietnam. Should the virus become readily transmissible from human to human, the disease could easily spread beyond Asia's borders and initiate a global pandemic. The U.S. population has no immunity and therefore no protection against this deadly virus.

Implications of Pandemic Influenza for the United States

The impact of a pandemic influenza outbreak cannot be overemphasized. During the past century, influenza pandemics occurred in 1918, 1957, and 1968, with significant morbidity and mortality in both high-risk and healthy children and adults. These outbreaks cost the lives of hundreds of thousands of Americans. Historians now estimate that between 50 million and 100 million people died as a result of the 1918 influenza pandemic alone. More than half a million Americans died, many of them young adults in the prime of life. Although the 1956 and 1968 pandemics were not as severe, the current mortality rate among patients with H5N1 influenza is more than 50 percent compared with 2.5 to 5 percent for the disastrous 1918 pandemic virus. The Centers for Disease Control and Prevention (CDC) has estimated that a pandemic as severe as the 1918

pandemic would cause between 0.9 and 2.2 million deaths and 4 million to 10 million hospitalizations in the United States.

The next pandemic will cause much economic and social chaos. There will be a dramatic impact on the U.S. and global economies, and potentially on civil order and international security. Consider the billions of dollars of economic impact of the severe acute respiratory syndrome (SARS) epidemic. SARS was trivial in size and scope compared with even a modest flu pandemic.

United States Is Not Adequately Prepared

Congress and the Administration have begun to realize the real threat that influenza poses to the United States as evident by the allocation of additional monies for influenza activities in recent years. The Administration has proposed an additional $120 million for influenza preparedness activities in the fiscal year 2006 budget to further strengthen pandemic influenza preparedness efforts. While welcome, this is a small investment. Additionally, the Department of Health and Human Services (HHS) recently proposed a thoughtful and scientifically based draft pandemic preparedness and response plan that lays out public health measures to counter a sudden worldwide influenza epidemic. IDSA has provided extensive comments on the plan and currently is participating on an HHS workgroup to develop specific policies and improve preparedness. CDC has worked to strengthen its scientific and epidemiologic capacity to respond. The National Institutes of Health (NIH) has begun efforts to develop vaccine for avian influenza and has increased support for other basic research.

IDSA recognizes and appreciates the increasing level of federal support for U.S. preparedness efforts. However, IDSA agrees with the Institute of Medicine and virtually all experts who have concluded that the United States is at present woefully unprepared to respond to the next flu pandemic.

Two promising strategies can decrease the impact of a flu pandemic. Vaccination is the primary strategy to prevent influenza during normal years and during a pandemic. The recent shortage of flu vaccine highlights the fragility of our nation's vaccine supply. We clearly need a greater capacity to produce vaccine. This means we must attract more vaccine manufacturers to produce influenza vaccine within our borders. It has been estimated that vaccinating the U.S. population against a pandemic flu strain might require 600 million doses of vaccine (two doses for each person might be needed). Even in a normal year, only 50 million to 60 million doses of vaccine can be manufactured in the United States. Counting doses of vaccine imported from abroad, about 90 million doses are used. In the best case, it will take four to six months to begin to produce a pandemic influenza vaccine. Unfortunately, only three influenza vaccine manufacturers currently produce flu vaccines for the U.S. market; only one of them produces its vaccine within the United States.

Antiviral drugs would be the only available agents for treatment and prevention in the early phase of a pandemic. However, adequate supplies will not be available unless decisive action is taken. Global production of these agents is modest. If antivirals are to be available in an emergency they would need to be stockpiled in advance.

Strengthening our pandemic influenza preparedness activities also will provide significant benefits during the typical "interpandemic" flu season when 36,000 American lives are lost and 200,000 are hospitalized each year. The same cannot be said for preparedness activities for intentional biological emergencies such as smallpox, which does not exist in nature, or anthrax, which is an extremely rare disease.

Potential Legislative and Administrative Solutions

Considering the significance of the threat, IDSA has identified the following short and long term strategies to strengthen the U.S. level of preparedness and response to both interpandemic and pandemic influenza.

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- Secure vaccine and antiviral supplies**.**

  Adequate supplies of antivirals and if possible vaccine, need to be in place *before* a pandemic strikes, along with a plan to distribute them. More must be done to bring additional manufacturers into the vaccine business, particularly to develop domestic based companies so that the United States is not dependent on foreign suppliers. Increased use of vaccine during interpandemic years is needed to increase the manufacturing capacity. Without this strengthened capacity, we will be unable to meet the high demand that will occur during an influenza pandemic.

  Stockpiles of antiviral drugs are also essential. IDSA has proposed a stockpile of antivirals sufficient to treat 50 percent of the U.S. population. This stockpile will help to reduce mortality and allow vital services such as medical care and emergency

services to continue. Clearly, the current stockpile, which could treat less than 2 percent of the U.S. population, is inadequate. The cost of developing an adequate stockpile cannot be paid for by shifting funds within HHS agencies; it will require a separate appropriation. Given the enormous burden of illness and death anticipated in a pandemic, however, this investment promises an excellent return. In addition, the entire production capacity for oseltamivir is located in Switzerland. As with influenza vaccines, IDSA fully supports the development of antiviral production capacities within the United States.

It is essential that we develop a specific strategy to distribute antiviral drugs and vaccines to states, local health departments, and points-of-care. We support the effort currently underway by the Pandemic Influenza Working Group of the National Vaccine Advisory Committee (NVAC) to provide detailed estimates of the priorities for use of antivirals and the amount of drug needed to reach different target groups. This will provide more precise estimates of the size and cost of a stockpile needed to provide a specific level of benefit.

- <u>Advance Research and Development of Antivirals and Vaccines.</u>

  Current manufacturing of influenza vaccine depends on egg-based technology that is 60 years old. It imposes limits on the ability to ramp up production and to work with strains that are lethal to eggs. Research and development of newer vaccines is vital. NIH has recently outlined funding for work on cell-culture based vaccine and for antigen-sparing approaches. These are vital efforts and should be accelerated. Equal attention needs to be paid to our ability to rapidly and safely license new technologies

to produce new vaccines for widespread use. Truly innovative vaccines could be developed that do not need to be redesigned each year. Investment in this research could be extremely important but will take many years to realize a benefit.

Research also is needed to develop new antivirals with anti-influenza activity. We are currently dependent on a single agent, oseltamavir (also known as Tamiflu, an antiviral produced by Roche Pharmaceuticals). In the event H5N1 becomes a pandemic strain, this vulnerability will be dangerous.

- Create tax incentives for U.S. vaccine and antiviral manufacturers.

  The United States does not have the manufacturing capacity to produce enough vaccine and antivirals to meet its needs in a pandemic. Tax credits should be offered to encourage companies to build new manufacturing facilities in this country so that the United States is not dependent on foreign suppliers. Tax incentives and patent extensions should be available for companies that conduct research and develop new anti-flu therapies.

- Guarantee a market for influenza vaccines.

  Most pharmaceutical companies have left the vaccine business because demand is extremely unpredictable. Even last season, when there was a severe shortage of vaccine, millions of doses of flu vaccine went unused. To secure vaccine supplies for future influenza outbreaks, the government needs to guarantee it will buy a set amount of vaccine each season, and buy back a percentage of unsold vaccine at the end of each season.

The Centers for Medicare and Medicaid Services (CMS) also has a critical role to play. The recent increase in the Medicare reimbursement for administration of flu vaccine, although long overdue, was a positive step. However, the current system still places physicians at financial risk, which may have consequences for patient access to vaccine. Physicians must purchase vaccine annually in advance of the flu season. Unused vaccine is then discarded at the end of the flu season. Physicians are not compensated for the unused product, which, of course, may make them less inclined to purchase vaccine in advance in future years. As all Medicare beneficiaries should receive annual influenza vaccine, CMS should consider how to purchase enough vaccine for Medicare patients in a manner that does not place physicians at risk.

- Strengthen liability protection during emergency outbreak response**.**

  In case of a declared influenza emergency, it will be vital to immunize and treat large numbers of people. Even rare adverse reactions following vaccination and treatment would become more common when hundreds of millions are treated, and accelerated approval of new vaccines and treatments might not uncover all rare adverse events. Health care workers and medical facilities administering vaccines or treatments, as well as the companies that make them, should be protected from lawsuits stemming from adverse events so long as they follow standard medical and manufacturing procedures. A compensation fund similar in structure to the Vaccine Injury Compensation Fund should be established to cover the medical costs and lost earnings of anyone who develops complications due to vaccination or treatment.

- Improve coordination, communication, and planning.

  Many federal, state, and local agencies have vital roles in preparedness, planning, and response. HHS should develop a detailed plan to coordinate pandemic response at all levels, from local to national to international, including links between federal authorities and clinicians throughout the country. HHS should also define CDC as the coordinating authority within the department. Moreover, there needs to be a clear ability to coordinate efforts between departments, including not only HHS, but also Defense, Agriculture (USDA), Homeland Security, and State.

- Require health care workers to be vaccinated.

  Unfortunately, health care workers caring for sick people often spread patients' infections. In 2002, only 36 percent of U.S. health care workers received influenza vaccine. To improve patient safety, prevent unnecessary deaths and disease, and provide an example to patients, we believe that annual flu vaccination should be required for all health care workers who have contact with patients, with options to waive vaccination after signing an appropriate waiver.

- Strengthen education.

  Health care workers and the public need to better understand the seriousness and potential impact of an influenza pandemic, as well as how to prevent and treat it.

- Commit to international pandemic preparedness.

  A coordinated international effort is vital. The United States should work with other countries, particularly those most vulnerable, on plans to ensure that they have sufficient antiviral and vaccine supplies to protect their populations.

- Strengthen the response of federal agencies.

  The Food and Drug Administration should "fast-track" vaccine and antiviral review, and streamline regulation of the manufacturing process. Congress should increase the CDC's budget for global surveillance to detect influenza strains with pandemic potential. The NIH budget also should be increased for research to identify and evaluate new methods to accelerate vaccine research and development. USDA should develop a plan for culling poultry or other livestock and compensating farmers in the event of a pandemic, if necessary.

Conclusion

The United States remains unprepared for pandemic influenza that could kill millions of Americans over a short period of time with little warning. We may not have much time. The United States needs a rational, integrated, and comprehensive plan that will ensure an effective response. We also need a better-coordinated approach, both domestically and globally. If IDSA's recommendations are implemented, our nation will be better prepared for both the next pandemic and for influenza outbreaks that occur every year. As Winston Churchill said: "It is not enough to say, 'We are doing our best.' You have got to succeed in doing what is necessary."

IDSA appreciates the opportunity to testify before the House Energy and Commerce Health Subcommittee today. We look forward to working with you in the coming months to develop federal legislation needed to strengthen U.S. efforts to prepare for the next influenza pandemic.

Thank you. I will be happy to answer any questions.